UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

THE REGENTS OF THE UNIVERSITY OF CALIFORNIA, ABBOTT MOLECULAR INC., and ABBOTT LABORATORIES INC.,

Plaintiffs,

v.

DAKO NORTH AMERICA, INC. and DAKO A/S,

Defendants.

/

No. C 05-03955 MHP

MEMORANDUM & ORDER
Re: Claim Construction

Plaintiffs The Regents of the University of California ("UC Regents"), Abbott Molecular Inc., and Abbott Laboratories Inc. (collectively, "Abbott") brought this patent infringement action against defendants Dako North America, Inc. and Dako A/S (collectively, "Dako"), alleging infringement of two United States patents related to in situ DNA hybridization. Now before the court are the parties' proposed claim constructions. Having considered the parties' arguments and submissions, and for the reasons set forth below, the court enters the following memorandum and order.

BACKGROUND

Abbott holds the two patents at issue in this lawsuit, U.S. Patent No. 5,447,841 (the "'841 patent") and U.S. Patent No. 6,596,479 (the "'479 patent"). The two asserted patents have substantially identical specifications but were issued almost eight years apart and have different claims.[1] Both patents relate generally to the identification of target genes in a tissue sample through

DNA hybridization. In DNA hybridization, sections of nucleic acid that are labeled, usually with a fluorescent dye ("hybridization probes"), are bonded to complementary "target" regions of chromosomal DNA—typically, sections which encode a protein of interest. See, e.g., '841 patent at cols. 2–3. The fluorescent label provides visual confirmation of the presence of the target gene. Id.

The basic technology involved in DNA hybridization predates the asserted patents. The inventions described in the asserted patents improve upon the prior art hybridization process by increasing its accuracy in two ways. First, in order to guarantee that a sufficient number of hybridization probes will bond to the target region, the patents describe the use of a "[h]eterogeneous . . . mixture of labeled nucleic acid fragments" that "results in a substantially uniform distribution of fragments hybridized to the chromosomal DNA." Id. at 4:2–9. Second, the patents describe the use of countermeasures that prevent hybridization probes from bonding to regions of the chromosomal DNA outside of the target region. Of particular concern are so-called "repeat" or "repetitive" sequences of DNA which occur throughout the chromosomes. When these repeat sequences are similar in structure to parts of the target regions, hybridization probes designed to attach to those parts of the target region may instead hybridize at many undesired locations. These countermeasures constitute the key advances in the asserted patents.

LEGAL STANDARD

Under Markman v. Westview Instruments, Inc., 517 U.S. 370, 389–90 (1996), the court construes the scope and meaning of disputed patent claims as a matter of law. The first step of this analysis requires the court to consider the words of the claims. Teleflex, Inc. v. Ficosca N. Am., 299 F.3d 1313, 1324 (Fed. Cir. 2002). According to the Federal Circuit, the court must "indulge a 'heavy presumption' that a claim term carries its ordinary and customary meaning." CCS Fitness, Inc. v. Brunswick Corp., 288 F.3d 1359, 1366 (Fed. Cir. 2002). To determine the ordinary meaning of a disputed term, the court may review a variety of sources, including the claims themselves, other intrinsic evidence including the written description and prosecution history, and dictionaries and treatises. Teleflex, 299 F.3d at 1325. The court must conduct this inquiry not from the perspective

of a lay observer, but rather "from the standpoint of a person of ordinary skill in the relevant art." Id. (citing Zelinski v. Brunswick Corp., 185 F.3d 1311, 1316 (Fed. Cir. 1999)).

Among the sources of intrinsic evidence, the specification is "the single best guide to the meaning of a disputed term." Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed. Cir. 1996). By expressly defining terms in the specification, an inventor may "choose[] to be his or her own lexicographer," thereby limiting the meaning of the disputed term to the definition provided in the specification. Johnson Worldwide Assocs., Inc. v. Zebco Corp., 175 F.3d 985, 990 (Fed. Cir. 1999). In addition,"[e]ven when guidance is not provided in explicit definitional format, "the specification may define claim terms 'by implication' such that the meaning may be 'found in or ascertained by a reading of the patent documents.'" Irdeto Access, Inc. v. Echostar Satellite Corp., 383 F.3d 1295, 1300 (Fed. Cir. 2004) (quoting Bell Atl. Network Servs., Inc v. Covad Commc'ns Group, Inc., 262 F.3d 1258, 1268 (Fed. Cir. 2001)). "The specification may also assist in resolving ambiguity where the ordinary and accustomed meaning of the words used in the claims lack sufficient clarity to permit the scope of the claim to be ascertained from the words alone." Teleflex, 299 F.3d at 1325. At the same time, the Federal Circuit has cautioned that the written description "should never trump the clear meaning of the claim terms." Comark Commc'ns, Inc. v. Harris Corp., 156 F.3d 1182, 1187 (Fed. Cir. 1998) (citations omitted); see also Tate Access Floors, Inc. v. Maxess Techs., Inc., 222 F.3d 958, 966 (Fed. Cir. 2000) ("Although claims must be read in light of the specification of which they are part, . . . it is improper to read limitations from the written description into a claim . . . .").

Likewise, the prosecution history may demonstrate that the patentee intended to deviate from a term's ordinary and accustomed meaning. Teleflex, 299 F.3d at 1326. "Arguments and amendments made during the prosecution of a patent application and other aspects of the prosecution history, as well as the specification and other claims, must be examined to determine the meaning of terms in the claims." Southwall Techs., Inc. v. Cardinal IG Co., 54 F.3d 1570, 1576 (Fed. Cir.), cert. denied, 516 U.S. 987 (1995). "In particular, 'the prosecution history (or file wrapper) limits the interpretation of claims so as to exclude any interpretation that may have been

disclaimed or disavowed during prosecution in order to obtain claim allowance.'" Teleflex, 299 F.3d at 1326 (quoting Standard Oil Co. v. American Cyanamid Co., 774 F.2d 448, 452 (Fed. Cir. 1985)).

Dictionary definitions and other objective reference materials available at the time that the patent was issued may also provide evidence of the ordinary meaning of a claim. Phillips v. AWH Corp., 415 F.3d 1303, 1322 (Fed. Cir. 2005) (en banc); Texas Digital Sys., Inc. v. Telegenix, Inc., 308 F.3d 1193, 1202 (Fed. Cir. 2002). A dictionary "has the value of being an unbiased source, accessible to the public in advance of litigation." Phillips, 415 F.3d at 1322 (internal quotation omitted). Thus, district courts "are free to consult such resources at any time in order to better understand the underlying technology and may also rely on dictionary definitions when construing claim terms, so long as the dictionary definition does not contradict any definition found in or ascertained by a reading of the patent documents." Vitronics, 90 F.3d at 1584 n.6. A court should be cautious, however, not to place too much reliance on dictionaries, as the resulting construction may be too broad. Phillips, 415 F.3d at 1321.

Federal Circuit decisions take a less favorable view of other forms of extrinsic evidence, such as expert testimony and prior art not cited in the specification or the prosecution history, noting that "claims should preferably be interpreted without recourse to extrinsic evidence, other than perhaps dictionaries or reference books, and that expert testimony should be received only for the purpose of educating the judge." EMI Group N. Am., Inc. v. Intel Corp., 157 F.3d 887, 892 (Fed. Cir. 1998), cert. denied, 526 U.S. 1112 (1999). Although "extrinsic evidence in general, and expert testimony in particular, may be used . . . to help the court come to a proper understanding of the claims[,] it may not be used to vary or contradict the claim language . . . . Indeed, where the patent documents are unambiguous, expert testimony regarding the meaning of a claim is entitled to no weight." Vitronics, 90 F.3d at 1584.

The Federal Circuit recently revisited the basic approach to claim construction in Phillips, which provides at least two pieces of additional guidance. First, the Federal Circuit rejected a line of cases suggesting that claim interpretation must begin with a dictionary definition of the disputed

terms. Phillips, 415 F.3d at 1320–21. Second, the Federal Circuit emphasized that claim terms must be interpreted in light of their context, especially the language used in other claims and the specification. See id. at 1321. Taken as a whole, Phillips appears to signal a small retreat from formalism and bright-line rules in claim construction. As a result, the court will focus primarily on the intrinsic record before it. Cases cited by the parties in support of fixed "rules" of claim construction will accordingly be given somewhat less weight.

DISCUSSION

The following chart summarizes the court's construction of the disputed terms. The full analysis supporting each construction is below.

Term	Construction
"heterogeneous mixture"	"a mixture of labeled fragments comprising many copies each of labeled fragments having different base compositions and/or sizes, such that application of the labeled fragments to a chromosome results in a substantially uniform distribution of fragments hybridized to the chromosomal DNA"
"heterogeneous mixture of labeled unique sequence nucleic acid fragments"	"a heterogeneous mixture of labeled nucleic acid fragments that includes unique sequence fragments"
"unique segments"	"stretches of nucleic acid occurring fewer than 10 times per haploid genome"
"unique sequence"	"an ordering of nucleotide bases occurring fewer than 10 times per haploid genome"
"repetitive sequence"	"an ordering of nucleotide bases which is not unique"

"sufficient to permit detection of hybridized labeled nucleic acid containing unique segments"	"sufficient to permit detection of the labeled nucleic acid containing unique segments hybridized to target chromosomal DNA"
"detecting the labeled nucleic acid fragments which are hybridized to the interphase chromosomal DNA to determine"	No further construction is necessary.

I. "heterogeneous mixture"

The phrase "heterogeneous mixture" appears throughout the shared Specification and the claims of the '479 patent. Abbott argues that the phrase, when applied to nucleic acid fragments, should be construed to mean "a mixture containing many copies each of fragments having different base compositions and/or sizes." Dako argues that the phrase should be construed to mean a "mixture of labeled nucleic acid fragments, such that application of the mixture to a chromosome results in a substantially uniform distribution of fragments (i.e., interrupted only be repetitive sequences) hybridized to the chromosomal DNA." The parties' constructions differ in two respects: Dako's construction requires that the heterogeneous mixture yield a substantially uniform distribution of fragments, and further requires that the uniform distribution cover only the unique portions of the chromosomal DNA.

Although claim construction generally begins with the plain meaning of claim terms as understood by one of ordinary skill in the art, a patentee is free to act as his own lexicographer to define terms used in the claims. Here, the Specification includes an express definition of "heterogeneous mixture":

> Heterogeneous in reference to the mixture of labeled nucleic acid fragments means that the staining reagents comprise many copies each of fragments having different base compositions and/or sizes, such that application of the staining reagent to a

> chromosome results in a substantially uniform distribution of fragments hybridized to the chromosomal DNA.

Spec. at 4:2–9. Both parties rely on this definition in advancing their proposed constructions.

With respect to the first difference in the parties' constructions, the definition in the specification supports Dako's argument that the mixture must result in a substantially uniform distribution of fragments hybridized to the chromosomal DNA. Indeed, Abbott appears to concede in its brief that the Specification "explain[s] that application of the heterogeneous mixture to a chromosome results in a substantially uniform distribution of fragments hybridized to the chromosomal DNA." The court therefore finds that the resulting distribution must be substantially uniform.

With respect to the second difference in the parties' construction, Dako's proposed definition would exclude heterogeneous mixtures which include some repetitive segments, a possibility expressly contemplated by the Specification: "preferably the heterogeneous mixtures are *substantially free* from so-called repetitive sequences." Spec. at 4:20–22 (emphasis added). The court therefore construes "heterogeneous mixture," when used in the context of labeled nucleic acid fragments, to mean "a mixture of labeled fragments comprising many copies each of labeled fragments having different base compositions and/or sizes, such that application of the labeled fragments to a chromosome results in a substantially uniform distribution of fragments hybridized to the chromosomal DNA."

II. "heterogeneous mixture of labeled unique sequence nucleic acid fragments"

The phrase "heterogeneous mixture of labeled unique sequence nucleic acid fragments" appears only in claim 1 of the '479 patent: "1. A method of staining target interphase chromosomal DNA . . ., the method comprising: (a) providing a heterogeneous mixture of **labeled unique sequence nucleic acid fragments** which are substantially complementary to nucleic acid segments within the interphase chromosomal DNA for which detection is desired . . ." '479 patent at 16:6–13 (emphasis added).

Abbott argues that the phrase should be construed to mean "labeled nucleic acid fragments that include unique sequences." Dako argues that the phrase should be construed to mean "fragments of labeled DNA or RNA that contain only unique sequences." The parties' constructions differ in only one respect: whether the mixture must consist entirely of unique sequences, or whether the mixture may also contain repetitive sequences.

The language of claim 1, standing alone, is ambiguous. The claim phrase recites a "mixture *of*" labeled unique sequence nucleic acid fragments, not a "mixture *comprising*" or a "mixture *consisting of*." Although the Federal Circuit has construed the similar phrase "composed of" narrowly, the word "of" does not have an established meaning as open or closed ended. See AFG Indus., Inc. v. Cardinal IG Co., 239 F.3d 1239, 1245 (Fed. Cir. 2001) (finding that "'composed of' in this case should be interpreted in the same manner as 'consisting essentially of' . . . [which excludes] ingredients that would materially affect the basic and novel characteristics of the claimed composition," but noting that transition phrases without established meaning "must be interpreted in light of the specification to determine whether open or closed claim language is intended.") The court must therefore look to the remainder of claim 1, the other claims of the '479 patent and the remainder of the intrinsic record for guidance.

The remainder of claim 1 provides some support for Dako's proposed construction. Element (a) indicates that the fragments are "designed to allow detection" of various characteristics of interest, such as "an extra or missing portion or portions of a chromosome." '479 patent at 16:13–14. Element (b) recites "employing the heterogeneous mixture [i.e., the mixture referenced in element (a)] . . . to permit detection of labeled nucleic acid fragments which are hybridized to interphase chromosomal DNA." Id. at 16:17–20. Finally, element (c) recites "detecting the labeled nucleic acid fragments which are hybridized to the interphase chromosomal DNA [i.e., the fragments recited in element (b)] to determine whether an extra or missing chromosome . . . is present in the target interphase chromosomal DNA." Id. at 16:24–29. As Dako correctly points out, if the heterogenous mixture includes a substantial number of repeat sequences, unless some form of blocking (not recited in claim 1) is employed, the fragments cannot be used to reliably detect the

presence or absence of particular chromosomes. According to Dako, the fact that the claim as construed by Abbott encompasses inoperative matter makes Abbott's proposed construction implausible.

It is true that "[c]laims which include a substantial measure of inoperatives . . . are fairly rejected under 35 U.S.C. § 112." In re Corkill, 771 F.2d 1496, 1501 (Fed. Cir. 1985); see also Graver Tank & Mfg. Co. v. Linde Air Prods. Co., 336 U.S. 271, 277 (1949), aff'd on reh'g, 339 U.S. 605 (1950) ("it is clear that [claims] fail equally to perform their function as a measure of the grant when they overclaim the invention."). The canon of construing claims to avoid invalidity, however, only applies when the record is otherwise in equipoise. See Phillips, 415 F.3d at 1327 ("we have limited the maxim [that claims should be construed to preserve their validity] to cases in which 'the court concludes, after applying all the available tools of claim construction, that the claim is still ambiguous.'").

Here, dependent claim 12 unambiguously indicates that the word "of" in claim 1 was intended to be open ended. Claim 12 recites "[t]he method of claim 1, wherein the heterogeneous mixture further comprises repetitive sequences." '479 patent at 16:57–58. Claim 13 adds to claim 12 "the step of disabling the hybridization capacity of repetitive sequences in the heterogeneous mixture." In order for claims 12 and 13 to be valid, claim 1 must allow for repetitive sequences in the heterogeneous mixture, and must further allow for them to be disabled through blocking. The parties do not dispute that claim 1 permits the addition of a blocking step, as a result of the express use of the word "comprising" between the preamble and the recited method steps. Claim 12 suggests that the word "of" should be read as "comprising" with respect to the contents of the heterogeneous mixture as well.

Dako also argues that the narrow claim language stands in contrast to broader language in the specification, which uses the phrase "heterogeneous mixture of labeled nucleic acid fragments" without the "unique sequence" modifier. See Spec. at 4:2–9. The heterogeneous mixture described in the specification includes fragments with unique sequences as well as fragments with repetitive sequences. See id. at 4:20–23 ("preferably the heterogeneous mixtures are substantially free from

so-called repetitive sequences, both the tandem variety and the interspersed variety"). As this passage makes clear, the mixture must include unique sequences (which bond to the region of interest) and may include repetitive sequences, but is preferably "substantially" free of repetitive sequences. Abbott's proposed construction for the claim language, which encompasses both unique and repetitive segments, is apparently coextensive with the broader phrase used in the Specification. Although the court is troubled by assigning the same meaning to different phrases, the unambiguous guidance provided by claim 12 is clearer than any inference which might be drawn from the inconsistent use of language.

Finally, Dako argues that the patentee gave up repetitive sequences during prosecuting. In responding to a rejection, the applicant stated that "'[u]nique sequence nucleic acid fragments are in contrast with, and free of, 'repetitive sequence' nucleic acid." Hoffman Dec., Exh. J at 7. The quoted statement is perfectly consistent with Abbott's proposed construction, which does not interpret "unique sequence . . . fragments" to include repetitive fragments, but rather depends on the word "of" for inclusion of repetitive sequence fragments in addition to the unique sequence fragments which are expressly recited in the claim.

The court therefore construes "heterogeneous mixture of labeled unique sequence nucleic acid fragments" to mean "a heterogeneous mixture of labeled nucleic acid fragments that includes unique sequence fragments."

III. "unique segments" / "unique sequence" / "repetitive sequence"

The parties' disputes with respect to the disputed terms "unique segments," "unique sequence" and "repetitive sequence" are related, and must be considered together.

With respect to "unique segments," Abbott proposes that the phrase be construed to mean "stretches of nucleic acid that contain sequences that occur 1 to 10 times in the haploid genome." Dako proposes that the phrase be construed to mean "stretches of DNA or RNA that contain only DNA or RNA sequences present in a single copy per haploid genome and are free of repetitive sequences."

With respect to "unique sequence," Abbott proposes that the phrase be construed to mean "nucleic sequence that occurs from 1 to 10 times in a haploid genome." Dako proposes that the phrase be construed to mean "stretch of DNA or RNA that contains only a DNA or RNA sequence present in a single copy per haploid genome and is free of repetitive sequences."

With respect to "repetitive sequence," Abbott proposes that the phrase be construed to mean "nucleic acid sequence that is not unique." Dako proposes that the phrase be construed to mean "stretch of DNA or RNA that contains only a DNA or RNA sequence that is not a unique sequence."

The parties' proposed constructions differ in two critical respects. First, Abbott argues that "segment" refers to an actual stretch of nucleic acid, while "sequence" refers to a particular ordering of bases and not to an actual physical piece of genetic material. Dako argues that both "segment" and "sequence" refer to a physical piece of nucleic acid. Second, Abbott argues that "unique" means "occur[ring] from 1 to 10 times in a haploid genome," while Dako argues that "unique" means "present in a single copy"—i.e., not 2–10 copies—per haploid.

A. "segments" vs. "sequence"

The phrase "unique segments" appears only in claim 1 of the '841 patent:

1. A method of staining target chromosomal DNA comprising:

(a) providing
1) labeled nucleic acid that comprises fragments which are substantially complementary to nucleic acid segments within the chromosomal DNA for which detection is desired, and
2) blocking nucleic acid that comprises fragments which are substantially complementary to repetitive segments in the labeled nucleic acid; and

(b) employing said labeled nucleic acid, blocking nucleic acid, and chromosomal DNA in in situ hybridization so that labeled repetitive segments are substantially blocked from binding to the chromosomal DNA, while hybridization of **unique segments** within the labeled nucleic acid to the chromosomal DNA is allowed, wherein blocking of the labeled repetitive segments is sufficient to permit detection of hybridized labeled nucleic acid containing **unique segments**, and wherein the chromosomal DNA is present in a morphologically identifiable chromosome or cell nucleus during the in situ hybridization.

'841 patent at 17:4–25. The word "segment," standing alone, appears throughout the claims of the '841 patent, in claim 1 of the '479 patent, in the Background of the Invention of the Specification, and in the title of prior art papers cited in the Specification. The word "segment" is consistently used to refer to a stretch of nucleic acid. Both parties are in agreement on this point. The court therefore construes the word "segment" to mean "a stretch of nucleic acid."

The phrase "unique sequence" appears throughout the claims of the '479 patent and the shared Specification. Claim 1 of the '479 patent is illustrative:

> 1. A method of staining target interphase chromosomal DNA to detect an extra or missing portion or portions of a chromosome . . . , the method comprising:
>
> > (a) providing a heterogeneous mixture of labeled **unique sequence** nucleic acid fragments which are substantially complementary to nucleic acid segments within the interphase chromosomal DNA for which detection is desired . . .

'479 patent at 16:6–29 (emphasis added). The word "sequence," standing alone, also appears numerous times in the claims of both patents, as well as throughout the Specification.

The word "sequence" and the phrase "unique sequence" are most often used as they are in claim 1 of the '479 patent—as modifiers for words describing physical sections of nucleic acid, such as "DNA," "nucleic acid," or "fragment." See, e.g., '479 patent at 16:9–10 ("unique sequence nucleic acid fragments"); id. at Abstract ("unique sequence regions of the chromosomal DNA"); id. at 3:39–40 ("unique sequence DNA fraction"). Occasionally the '479 patent uses the phrase "unique sequence" or the word "sequence," standing alone, to refer to a section of nucleic acid with a unique sequence of base pairs. See '479 patent at 16:56–57 ("wherein the heterogeneous mixture further comprises repetitive sequences"); id. at 7:4–5 ("The poly(dA) tail is used to separate the labeled unique sequence DNA from the unlabeled unique sequences").

In the context of claim 1 of the '479 patent, the phrase "unique sequence" is used as a modifier, referring to an ordering of bases rather than an actual snippet of DNA. The phrase "unique sequence" modifies "nucleic acid fragments," which are stretches of DNA or RNA. If Dako's proposed construction of "sequence" were correct, the claim would read "a heterogeneous mixture of *labeled unique sequences* which are substantially complementary to nucleic acid segments within

the interphase chromosomal DNA" instead of "a heterogeneous mixture of labeled *unique sequence nucleic acid fragments* which are substantially complementary to nucleic acid segments within the interphase chromosomal DNA."

Dako argues that the patentee stated during prosecution that "sequence" and "segment" have the same definition. Hoffman Dec., Exh. G at 4. During prosecution, a prior version of claim 1 did use the word "sequence" to refer to a stretch of DNA, rather than a particular order of bases. Id. at 1 (claiming "labeled nucleic acid that comprises fragments which are substantially complementary to nucleic acid [*sequences*] . . . within the chromosomal DNA.") (emphasis added). As currently used in the claims and Specification, however, the term "sequence," almost without exception, refers to an ordering of bases. Within claim 1, in particular, the meaning is clear.

The court therefore construes the term "sequence" to mean "an ordering of nucleotide bases."

B. "unique"

The word "unique," which the parties agree has a meaning opposite that of "repetitive" or "repeat," is used throughout the specifications and claims. As with the term "heterogeneous mixture," the specification of the '841 patent includes an express definition of "repetitive":

> As discussed more fully below, preferably the heterogeneous mixtures are substantially free from so-called repetitive sequences, both the tandem variety and the interspersed variety (see Hood et al., *Molecular Biology of Eucaryotic Cells* (Benjamin/Cummings Publishing Company, Menlo Park, Calif., 1975) for an explanation of repetitive sequences). Hood et al. states at pages 47-48 that "[e]ucaryotic sequences can be divided somewhat arbitrarily into three general frequency classes, termed highly repetitive (also called satellite DNA), middle-repetitive, and unique." Hood et al. indicates at page 49 that "[h]ighly repetitive DNA sequences are located in regions of centromeric heterochromatin", and at page 50 that "[m]iddle-repetitive sequences are interspersed among unique sequences."

'841 patent at 4:20–34. The Hood treatise, which is incorporated into both patents by reference, also defines the term "unique," though not with ideal clarity. On page 47, Hood states that "[s]equences represented only once in the genome (unique sequences) will hybridize slowly compared to sequences that are present in many copies." Hoffman Dec. Exh. R at 47. The table on page 47 also indicates that "Unique" sequences have only one copy per genome. Id. The same table, however,

indicates that "Middle-repetitive" sequences have between 10^1 and 10^5 copies per genome—leaving sequences occurring between 2 and 9 times per genome unclassified. Id. Abbott's proposed construction exploits this gap, defining "unique" as occurring from 1 to 10 times in a haploid genome." Dako's proposed construction is based on the express wording of Hood, which equates "unique" with "represented only once in the genome."

The conventional meaning of the word "unique" supports Dako's construction. A contemporaneous dictionary defines "unique" as "[b]eing the only one of its kind; solitary; sole." Hoffman Dec., Exh. S at 1400. The Specification also suggests that "unique" means "single": "Clones carrying unique sequence inserts are recognized as those that produce a single band during Southern analysis." Spec. at 9:55–57.

Abbott does not offer a contrary dictionary definition, but argues that one of ordinary skill in the art would understand that "unique" sequences can appear a handful of times in a genome without being considered "repetitive." For example, Abbott notes that the gene for hemoglobin, which is classified as "unique" in the Hood reference, was known at the time of the patent to occur more than once per haploid genome. See Hoffman Dec., Exh. R at 37; cf. Harper Dec., Exhs. O, P. Abbott also notes that the target sequences discussed in the specification are present in multiple copies per haploid.

Abbott's cited evidence, which is intrinsic to the patent because it appears in materials incorporated into the Specification by reference, indicates that one of ordinary skill in the art would have understood that "unique" is not as strict as its general dictionary definition would suggest. The specification and claims do not provide any clear motivation to limit the meaning as Dako suggests. The court therefore construes "unique" to mean "occurring fewer than 10 times per haploid genome."

IV. "sufficient to permit detection of hybridized labeled nucleic acid containing unique segments"

The phrase "sufficient to permit detection of hybridized labeled nucleic acid containing unique segments" appears in claim 1 of the '841 patent:

> (b) employing said labeled nucleic acid, blocking nucleic acid, and chromosomal DNA in in situ hybridization so that labeled repetitive segments are substantially blocked from binding to the chromosomal DNA, while hybridization of unique segments within the labeled nucleic acid to the chromosomal DNA is allowed, wherein blocking of the labeled repetitive segments is **sufficient to permit detection of hybridized labeled nucleic acid containing unique segments**, and wherein the chromosomal DNA is present in a morphologically identifiable chromosome or cell nucleus during the in situ hybridization.

'841 patent at 17:13–25 (emphasis added).

Abbott argues that the phrase should be construed to mean "makes it possible to ascertain in a single chromosome or in a single cell nucleus the presence of labeled nucleic acid that includes unique segments hybridized to target unique sequences in the chromosomal DNA." Dako argues that the phrase should be construed to mean "sufficient to permit detection of the labeled nucleic acid containing unique segments hybridized to target chromosomal DNA in a morphologically identifiable chromosome or cell nucleus." The parties' constructions differ in only one respect: whether the hybridization and detection must take place in a morphologically identifiable chromosome or cell nucleus.

Abbott argues that Dako's inclusion of the "morphologically identifiable chromosome or cell nucleus" limitation is redundant in light of the following phrase, which requires that the hybridization take place in a morphologically identifiable chromosome or cell nucleus. Id. at 17:22–25. The court agrees that Dako's proposed language is redundant; the claim already expressly requires that the hybridization take place in a morphologically identifiable chromosome or cell nucleus, and further that the hybridization take place to an extent "sufficient to permit detection of hybridized labeled nucleic acid containing unique segments," in the same morphologically identifiable cell nucleus.

Abbott's construction is also redundant in that it repeats that hybridization and detection must take place "in a single chromosome or in a single cell nucleus." The parties have agreed that the phrase "a morphologically identifiable . . . cell nucleus" is singular.

The court therefore construes "sufficient to permit detection of hybridized labeled nucleic acid containing unique segments" to mean "sufficient to permit detection of the labeled nucleic acid containing unique segments hybridized to target chromosomal DNA."

V. "detecting the labeled nucleic acid fragments which are hybridized to the interphase chromosomal DNA to determine"

The phrase "detecting the labeled nucleic acid fragments which are hybridized to the interphase chromosomal DNA to determine" appears in claim 1 of the '479 patent:

> (c) **detecting the labeled nucleic acid fragments which are hybridized to the interphase chromosomal DNA to determine** whether an extra or missing portion or portions of a chromosome, or a translocation or an inversion of a portion or portions of a chromosome is present in the target interphase chromosomal DNA.

'479 patent at 16:24–29 (emphasis added).

Abbott argues that the phrase should be construed to mean "ascertaining in a single cell nucleus the presence of labeled nucleic acid hybridized to the target unique sequence in the interphase DNA to determine . . ." Dako argues that the phrase should be construed to mean "detecting the labeled nucleic acid containing only unique segments hybridized to target interphase chromosomal DNA in a morphologically identifiable cell nucleus to decide or settle conclusively and authoritatively . . ." The parties' constructions differ in three respects. First, Dako's construction expressly requires that the labeled nucleic acid contain only unique segments. Second, Dako's construction requires that the hybridization take place in a morphologically identifiable cell nucleus. Third, Dako's construction requires that the determination be "conclusive" and "authoritative."

The "labeled nucleic acid fragments" recited in element (c) of claim 1 constitute a subset of the heterogeneous mixture of fragments recited in element (a); the fragments in element (c) have been "hybridized to the interphase chromosomal DNA." '479 patent at 16:25. The parties do not dispute that for detection to be possible, the vast majority of hybridized fragments must be unique sequence fragments. This requirement is implicit in Abbott's proposed construction, which requires

that the hybridization be to "the target unique sequence in the interphase DNA." Dako further concedes, both in its papers and at argument, that the binding of a very small number of fragments to repetitive sections of the chromosomal DNA will not prevent detection. Given the undisputed understanding that the vast majority of fragments bonded to the chromosomal DNA must be unique sequence fragments, Dako's "containing only unique segments" limitation, which is too narrow in any case, is not needed.

Nor do the parties dispute that the hybridization—and subsequent detection—must occur in a morphologically identifiable cell nucleus. The construction of that phrase, which the parties continue to vigorously dispute, is currently at issue in the appeal of the court's ruling on Abbott's motion for a preliminary injunction.

The remaining dispute centers on the meaning of the word "determine." Abbott argues that claim 1 does not require that one using the claimed process determine anything conclusively by examining a single cell, but rather permits the determination to involve review of multiple cells. Abbott cites Oncor in support of its contention. The defendant in Oncor argued that researchers using the accused method "do not use its technology to 'look at' a single chromosome or cell nucleus when identifying the location of a stain," and thus did not infringe claim 1 of the '841 patent. Oncor, 44 U.S.P.Q.2d at 1334. The court rejected this argument, noting that the claim "focuses on the objective results of the chromosome-staining process, not the activities of researchers who monitor those results." Id. Instead, the claimed process "mandates that the target DNA be present and detectable on a single chromosome or cell nucleus." Id. In other words, the claimed process must permit accurate determination for each cell examined, but a researcher may aggregate the results from examining multiple cells in order to make a more global diagnosis.

The reasoning of the Oncor court does not help Abbott for two reasons. First, the Oncor court expressly held that the process claimed in the '841 patent must yield "objective" results for each cell to which it is applied. Second, claim 1 of the '479 patent requires more than claim 1 of the '841 patent. In addition to requiring "detect[ion]," the '479 patent requires "determin[ing] whether an extra or missing portion or portions of a chromosome, or a translocation or an inversion of a

portion or portions of a chromosome is present in the target interphase chromosomal DNA." Abbott does not dispute that this determination must take place in a morphologically identifiable cell nucleus, which per the parties' stipulated construction (and the construction of the Oncor court) is a *single* cell nucleus. Claim 1 of the '479 patent thus requires, based on its plain language, a determination through the examination of a single cell.

Adding the words "conclusive" and "authoritative" to the definition does not add clarity, and lacks support in the intrinsic record. Indeed, neither party's construction adds clarity to the existing claim language. Other than the clarification that "determine" means "determine," for each cell on which the claimed method is performed, no further construction is necessary.

CONCLUSION

For the foregoing reasons, the court hereby construes the disputed terms as set forth in the table above.

IT IS SO ORDERED.

Dated: July 3, 2006

MARILYN HALL PATEL
District Judge
United States District Court
Northern District of California

ENDNOTES

1. As the two patents share a specification, citations will be to the column and line numbering for the specification for the '841 patent, hereinafter referred to as "Specification" or "Spec.", unless otherwise noted.